Efficacy of intravitreal pegcetacoplan in geographic atrophy: results from the DERBY and OAKS trials

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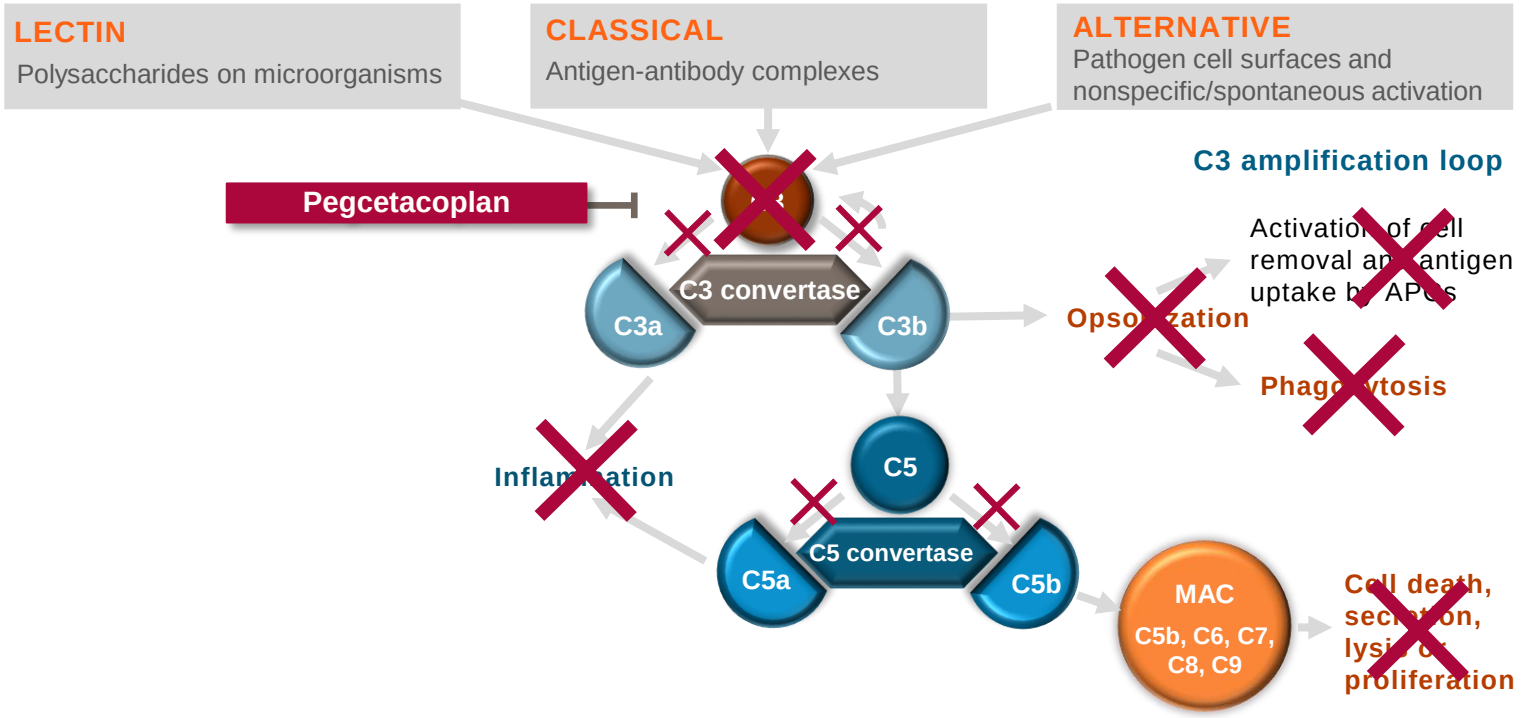
Pegcetacoplan is an investigational product in geographic atrophy. The treatment discussed in the presentation is not an FDA-approved use of pegcetacoplan.

Disclosures

- Dr. Steinle is a consultant or has received financial support from Apellis, Genentech, and Novartis.
- Studies funded by Apellis Pharmaceuticals

Introduction

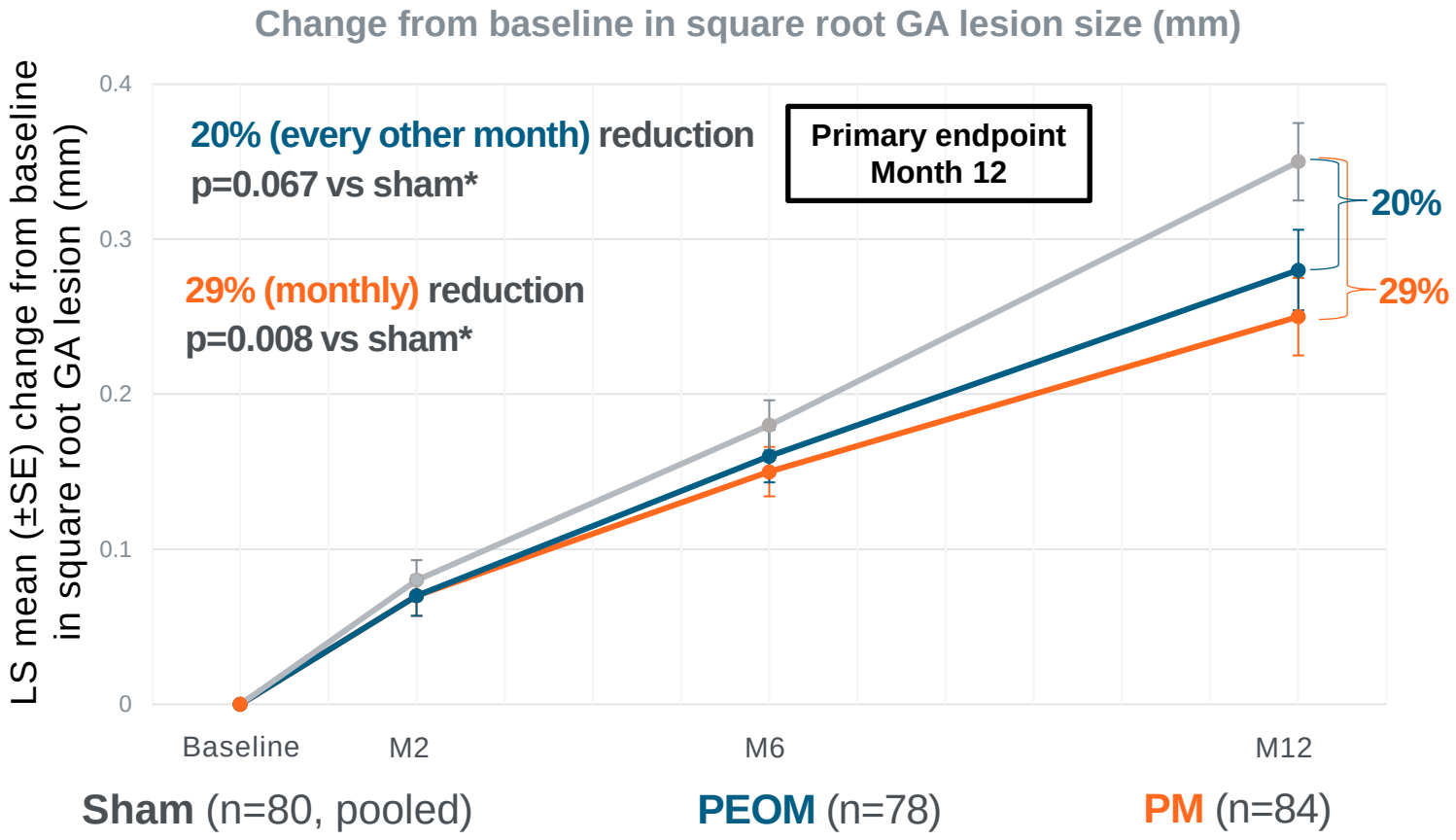


- Dysregulation of the complement cascade has been implicated in GA pathogenesis
- All 3 complement pathways end in the central cleavage of C3
- Pegcetacoplan is a pegylated, highly-selective peptide that binds C3, preventing its cleavage
- Inhibition of C3 blocks steps in the complement cascade needed for opsonization, inflammation, and formation of MAC

Figure adapted from Ricklin D, et al. Immunol Rev 2016;274(1):33–58.
APC=antigen-presenting cell; GA=geographic atrophy; MAC=membrane attack complex.
Liao DS, et al. Ophthalmology 2020;127:186–95.

Introduction and objective

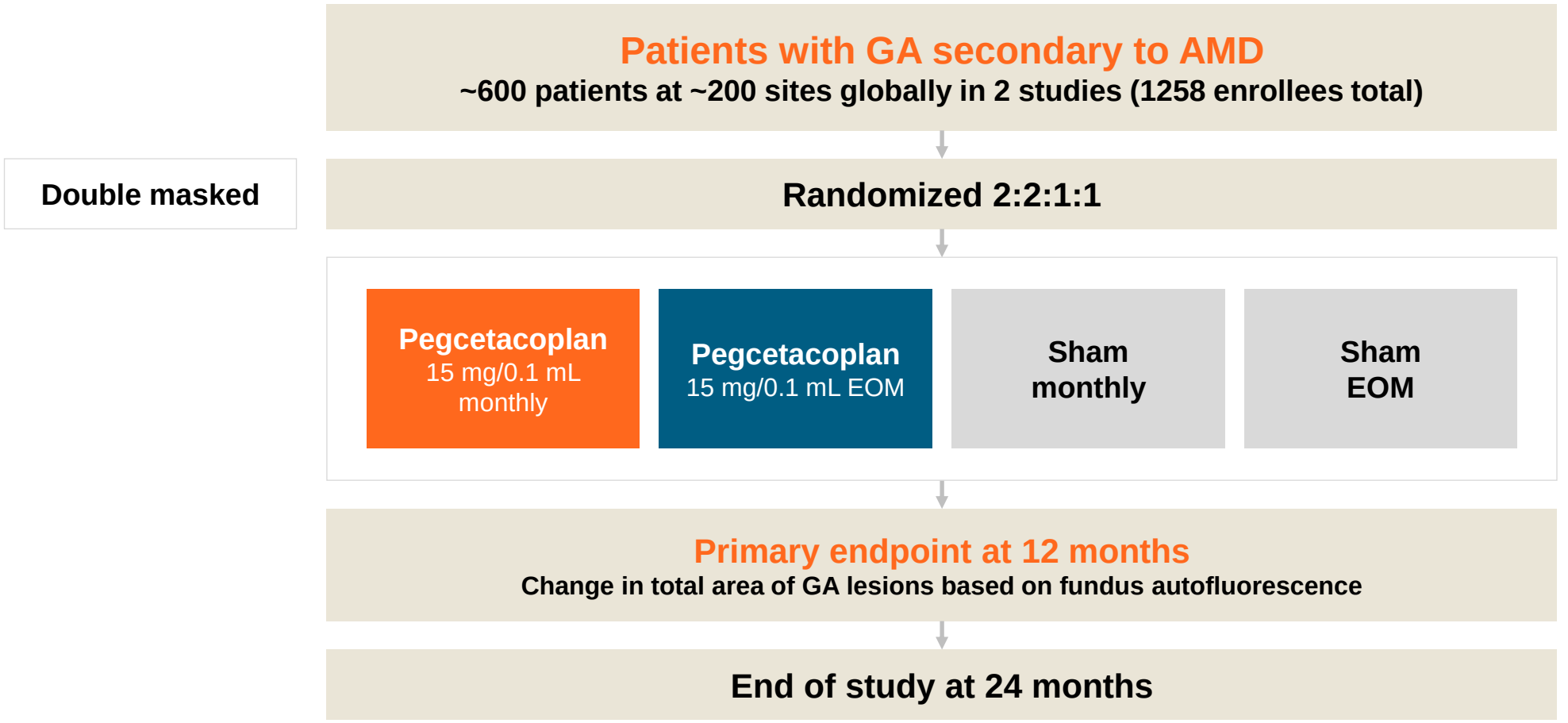
Phase 2 FILLY Results



- **Phase 3 DERBY & OAKS objective:** to assess the efficacy and safety of multiple intravitreal injections of pegcetacoplan in patients with GA secondary to AMD

*P<0.1 was the predefined threshold for statistical significance in FILLY.
AMD=age-related macular degeneration; GA=geographic atrophy; LS=least squares; M=Month; PEOM=pegcetacoplan every other month; PM=pegcetacoplan monthly; SE=standard error.
Liao DS, et al. Ophthalmology 2020;127:186–95.

Global phase 3 program: Design of studies



Protocol study number, APL-2 303 (DERBY); NCT03525600

Protocol study number, APL-2 304 (OAKS); NCT03525613

AMD=age-related macular degeneration; EOM=every other month; GA=geographic atrophy.

Key inclusion and exclusion criteria

Key inclusion criteria

- Age ≥60 years
- BCVA ≥24 letters ETDRS (20/320 Snellen equivalent)
- GA lesion requirements:
  - Total size: ≥2.5 and ≤17.5 mm^2
  - Foveal and extrafoveal GA allowed
  - If multifocal, at least 1 focal lesion must be ≥1.25 mm^2 (0.5 DA)
  - Presence of perilesional hyperautofluorescence

Key exclusion criteria

- GA secondary to a condition other than AMD, such as Stargardt disease in either eye
- Ocular history of or active CNV in the study eye, including presence of RPE tear (assessed by reading center)

Ocular history of active CNV in the fellow eye is not exclusionary

AMD=age-related macular degeneration; BCVA=best-corrected visual acuity; CNV=choroidal neovascularization; DA=disc area; ETDRS=Early Treatment Diabetic Retinopathy Study; GA=geographic atrophy; RPE=retinal pigment epithelium.

Key endpoints

Primary

- Change from baseline to Month 12 in total area of GA lesion(s) in the study eye (in mm^2) based on FAF

Secondary (prespecified analyses to be conducted at 24 months)

- BCVA, LL-BCVA, low-luminance deficit
- Reading speed
- Microperimetry (OAKS study only*) — Macular Integrity Assessment (MAIA) device
- National Eye Institute Visual Functioning Questionnaire 25-Item Version (NEI VFQ-25)
- Functional Reading Independence Index (FRI) composite score

*Patients must meet following criteria: (a) able to detect fixation target, (b) total elapsed time to complete 68-point exam <30 min, (c) reliability test ratio <20%, (d) willing and able to undertake microperimetry in investigator's opinion.

BCVA=best-corrected visual acuity; FAF=fundus autofluorescence; GA=geographic atrophy; LL-BCVA=low-luminance BCVA.

Key demographics and baseline study eye characteristics

		OAKS		
Characteristic		PM (N=202)	PEOM (N=205)	Sham Pooled (N=206)
Age, mean (SD)		78.8 (7.24)	78.1 (7.74)	78.6 (7.26)
Female, n (%)		125 (61.9%)	117 (57.1%)	133 (64.6%)
Male, n (%)		77 (38.1%)	88 (42.9%)	73 (35.4%)
Geographic region				
US, n (%)		147 (72.8%)	142 (69.3%)	147 (71.4%)
ROW, n (%)		55 (27.2%)	63 (30.7%)	59 (28.6%)
Caucasian, n (%)		185 (91.6%)	189 (92.2%)	187 (90.8%)
GA lesion size (mm^2), mean (SD)		8.18 (3.893)	8.29 (3.904)	8.20 (3.722)
Square root GA lesion size (mm), mean (SD)		2.78 (0.682)	2.80 (0.674)	2.79 (0.649)
GA lesion size, n (%)	<7.5 mm^2	101 (50.0%)	99 (48.3%)	104 (50.5%)
GA lesion location, n (%)	Extrafoveal	86 (42.6%)	74 (36.1%)	60 (29.1%)
GA lesion focality, n (%)	Unifocal	59 (29.2%)	62 (30.2%)	68 (33.0%)
Intermediate/large drusen, n (%)	>20	93 (46.0%)	104 (50.7%)	103 (50.0%)
NL-BCVA (ETDRS letters), mean (SD)		61.0 (15.30)	58.2 (17.03)	57.5 (16.57)

These analyses were performed on the modified intention-to-treat (mITT) population. The mITT population was defined as all randomized patients who received at least 1 injection of pegcetacoplan or sham and have baseline and at least 1 post-baseline value of GA lesion area in the study eye.

GA=geographic atrophy; mm=millimeters; n=number of patients; NL-BCVA=normal luminance best-corrected visual acuity; PM=pegcetacoplan monthly; PEOM=pegcetacoplan every other month; ROW=rest of world; SD=standard deviation; US=United States.

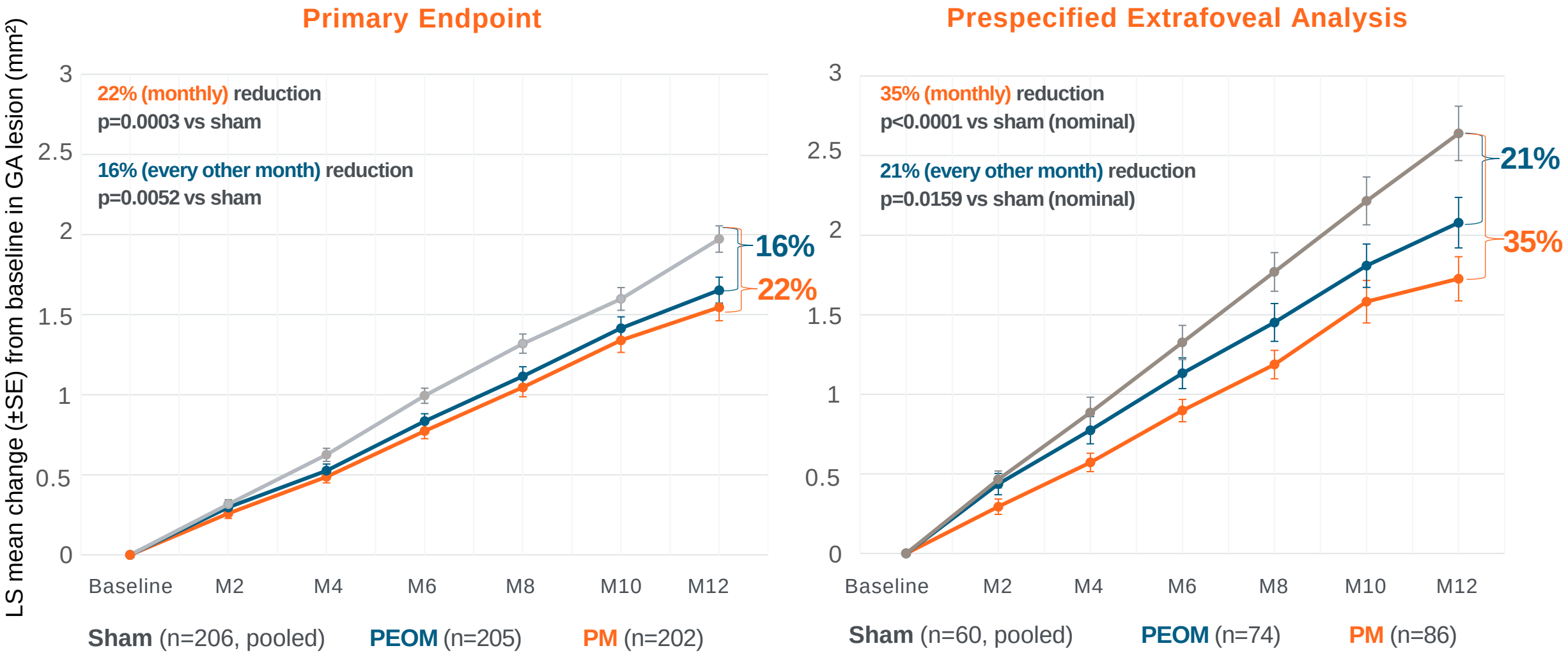
Key demographics and baseline study eye characteristics

		DERBY		
Characteristic		PM (N=201)	PEOM (N=200)	Sham Pooled (N=194)
Age, mean (SD)		78.7 (6.91)	79.2 (7.07)	78.6 (7.29)
Female, n (%)		118 (58.7%)	120 (60.0%)	122 (62.9%)
Male, n (%)		83 (41.3%)	80 (40.0%)	72 (37.1%)
Geographic region				
US, n (%)		142 (70.6%)	122 (61.0%)	122 (62.9%)
ROW, n (%)		59 (29.4%)	78 (39.0%)	72 (37.1%)
Caucasian, n (%)		187 (93.0%)	185 (92.5%)	187 (96.4%)
GA lesion size (mm^2), mean (SD)		8.36 (4.182)	8.22 (3.886)	8.26 (4.260)
Square root GA lesion size (mm), mean (SD)		2.80 (0.723)	2.79 (0.677)	2.78 (0.734)
GA lesion size, n (%)	<7.5 mm^2	99 (49.3%)	98 (49.0%)	94 (48.5%)
GA lesion location, n (%)	Extrafoveal	72 (35.8%)	81 (40.5%)	73 (37.6%)
GA lesion focality, n (%)	Unifocal	54 (26.9%)	53 (26.5%)	66 (34.0%)
Intermediate/large drusen, n (%)	>20	78 (38.8%)	78 (39.0%)	98 (50.5%)
NL-BCVA (ETDRS letters), mean (SD)		59.5 (17.40)	58.9 (15.97)	59.1 (16.85)

These analyses were performed on the modified intention-to-treat (mITT) population. The mITT population was defined as all randomized patients who received at least 1 injection of pegcetacoplan or sham and have baseline and at least 1 post-baseline value of GA lesion area in the study eye.

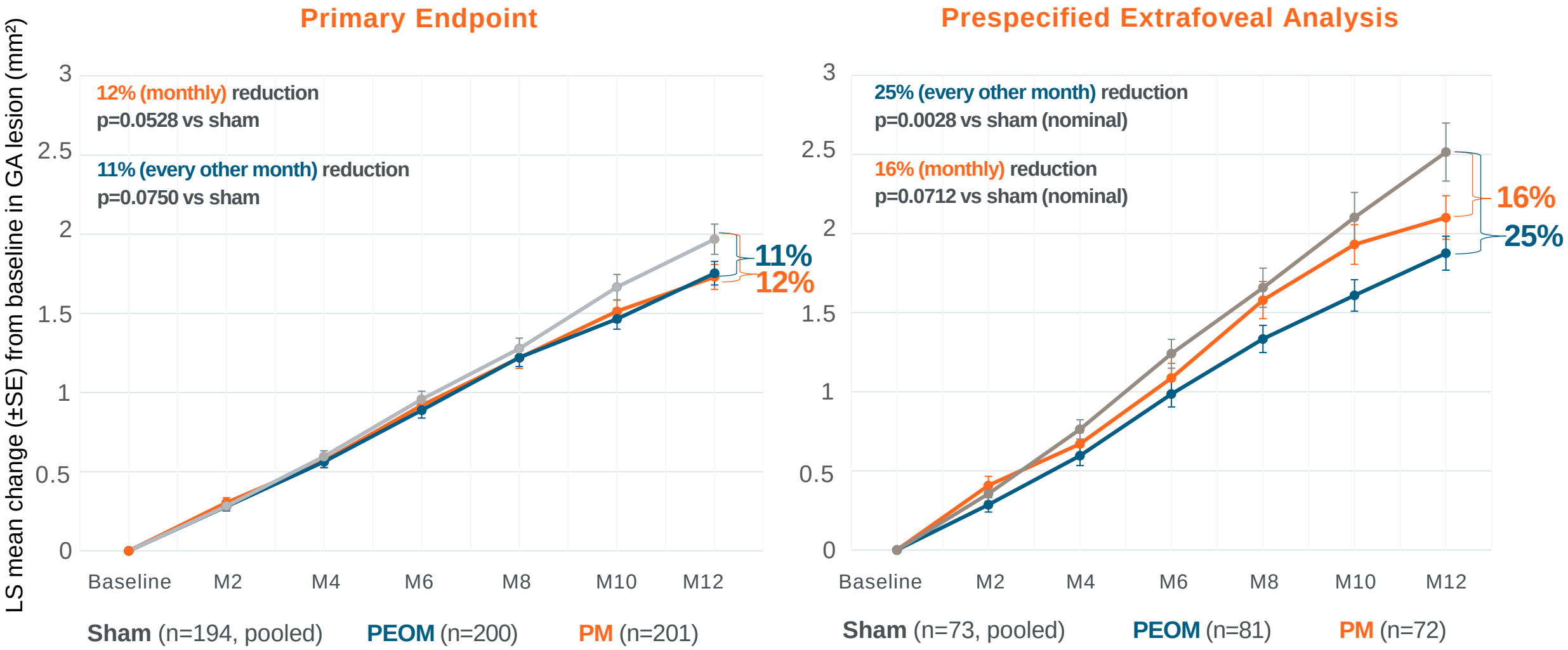
GA=geographic atrophy; mm=millimeters; n=number of patients; NL-BCVA=normal luminance best-corrected visual acuity; PM=pegcetacoplan monthly; PEOM=pegcetacoplan every other month; ROW=rest of world; SD=standard deviation; US=United States.

OAKS: Pegcetacoplan met the primary endpoint and further reduced lesion growth in patients with extrafoveal lesions



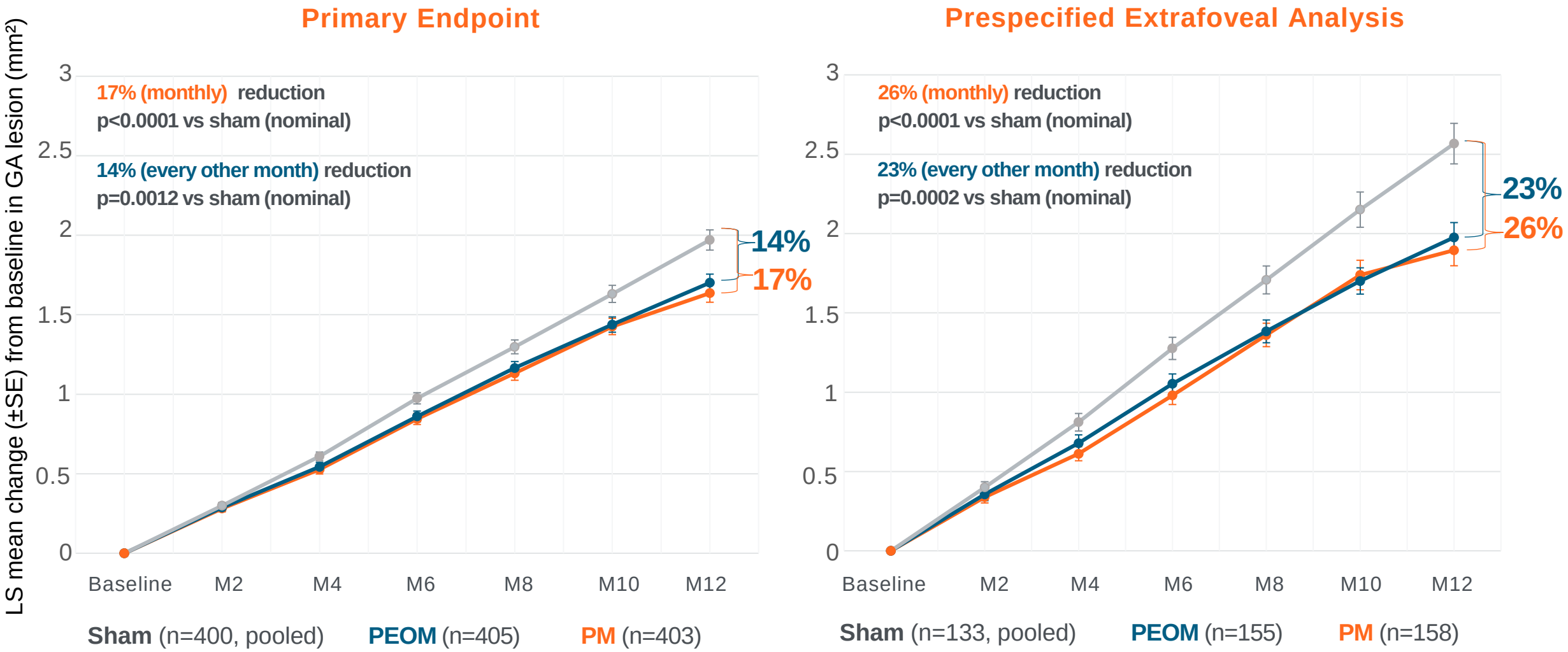
LS means estimated from a mixed-effects model for repeated measures. The modified intention-to-treat population was used for the analysis.
GA=geographic atrophy; LS=least square; M=month; PEOM=pegcetacoplan every other month; PM=pegcetacoplan monthly; SE=standard error.

DERBY: Pegcetacoplan did not meet the primary endpoint and reduced lesion growth in patients with extrafoveal lesions



LS means estimated from a mixed-effects model for repeated measures. The modified intention-to-treat population was used for the analysis.
GA=geographic atrophy; LS=least square; M=month; PEOM=pegcetacoplan every other month; PM=pegcetacoplan monthly; SE=standard error.

OAKS and DERBY: Pegcetacoplan reduced lesion growth in prespecified combined analyses of the primary endpoint and in extrafoveal lesions



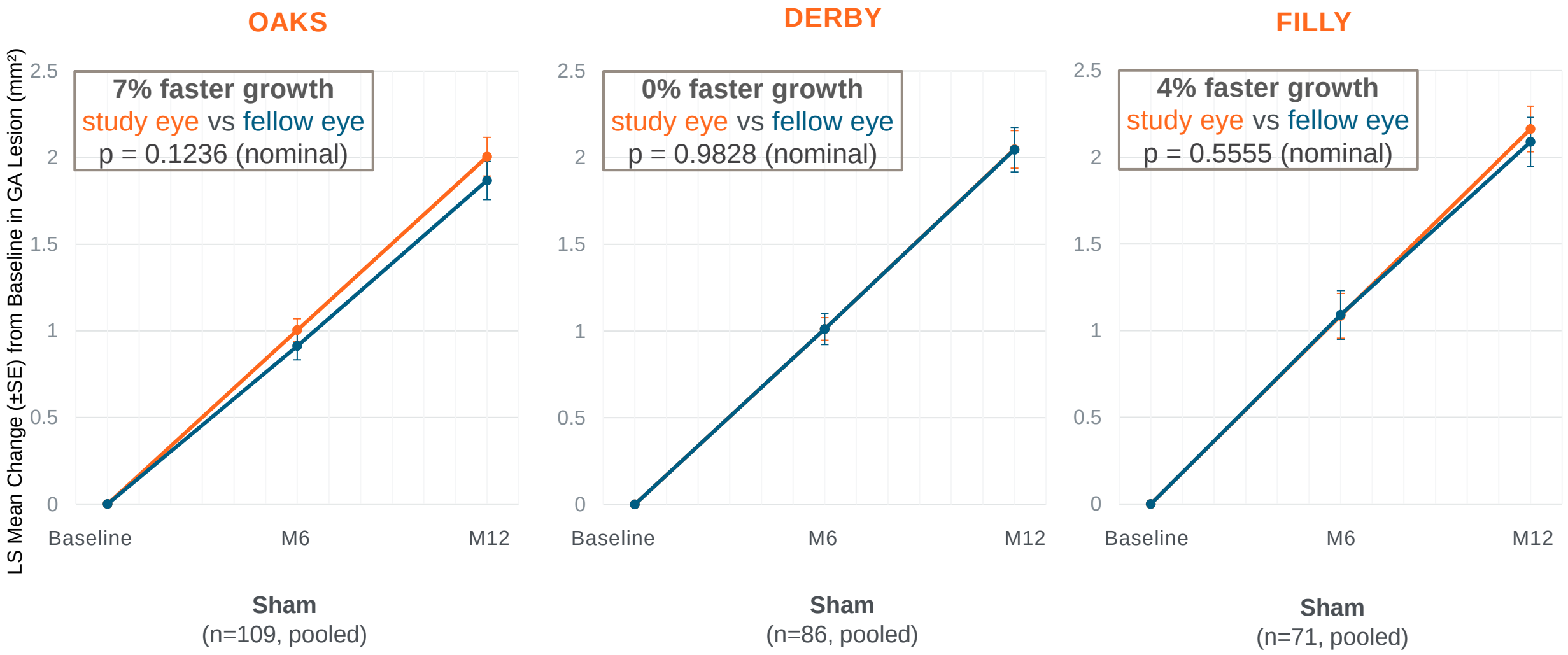
LS means estimated from a mixed-effects model for repeated measures. The modified intention-to-treat population was used for the analysis.
GA=geographic atrophy; LS=least square; M=month; PEOM=pegcetacoplan every other month; PM=pegcetacoplan monthly; SE=standard error.

Analysis of **fellow eye** vs **study eye** lesion growth

- Patients with bilateral GA were included in this analysis of DERBY and OAKS
- In addition, for a subject to be included, the fellow eye had to meet the following criteria:
  - Absence of CNV in the medical history
  - Baseline GA lesion size between 2.5 and 17.5 mm^2
  - Presence of any pattern of hyperautofluorescence in the junctional zone of GA
  - GA not confluent with peripapillary atrophy
- For FILLY, all bilateral GA patients are included due to lower sample size
- Effect sizes can differ from sham-controlled analysis due to potential fellow eye drug effect

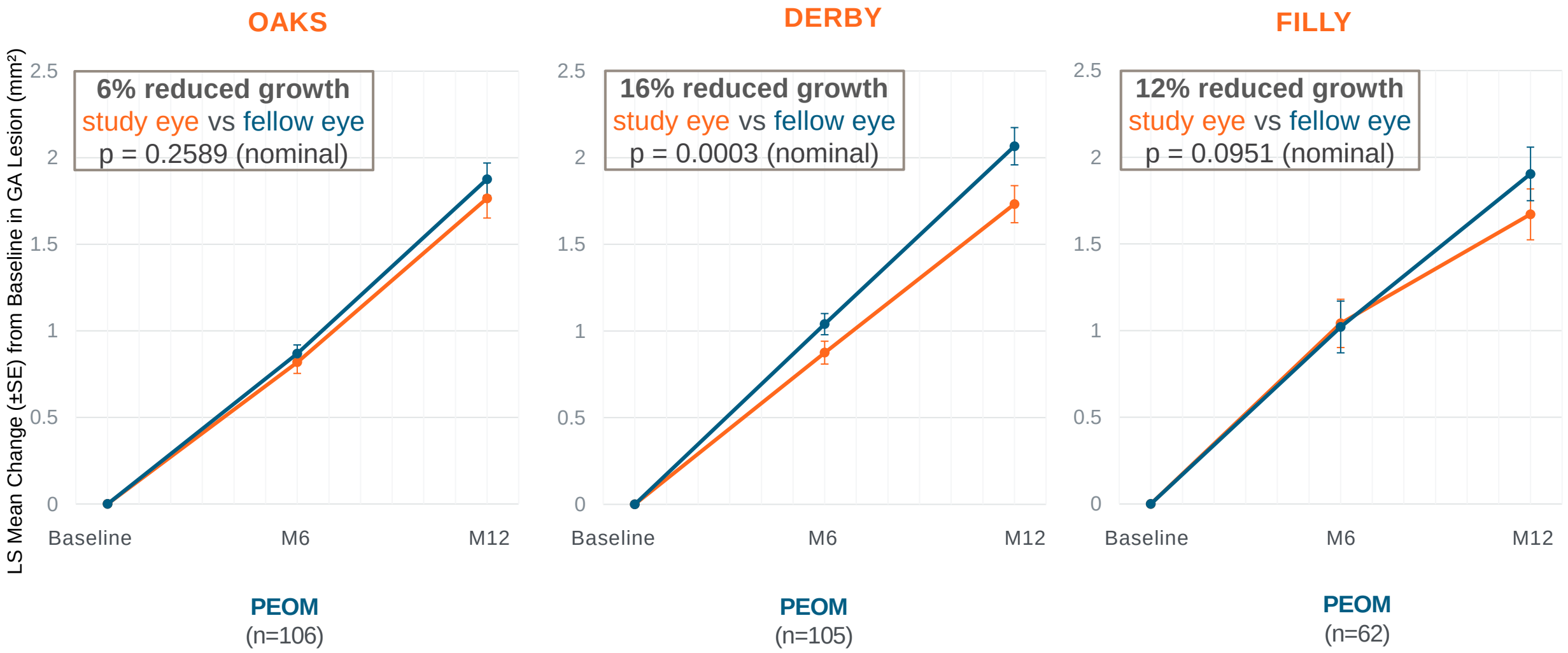
CNV=choroidal neovascularization; GA=geographic atrophy.

Balanced lesion growth in study eyes vs. fellow eyes in **sham pooled** groups



LS means estimated from a mixed-effects model for repeated measures. The mITT population was used for the analysis.
GA=geographic atrophy; LS=least square; M=month; PEOM=pegcetacoplan every other month; PM=pegcetacoplan monthly; SE=standard error.

Pegcetacoplan **every other month** reduced lesion growth in treated study eyes vs. untreated fellow eyes



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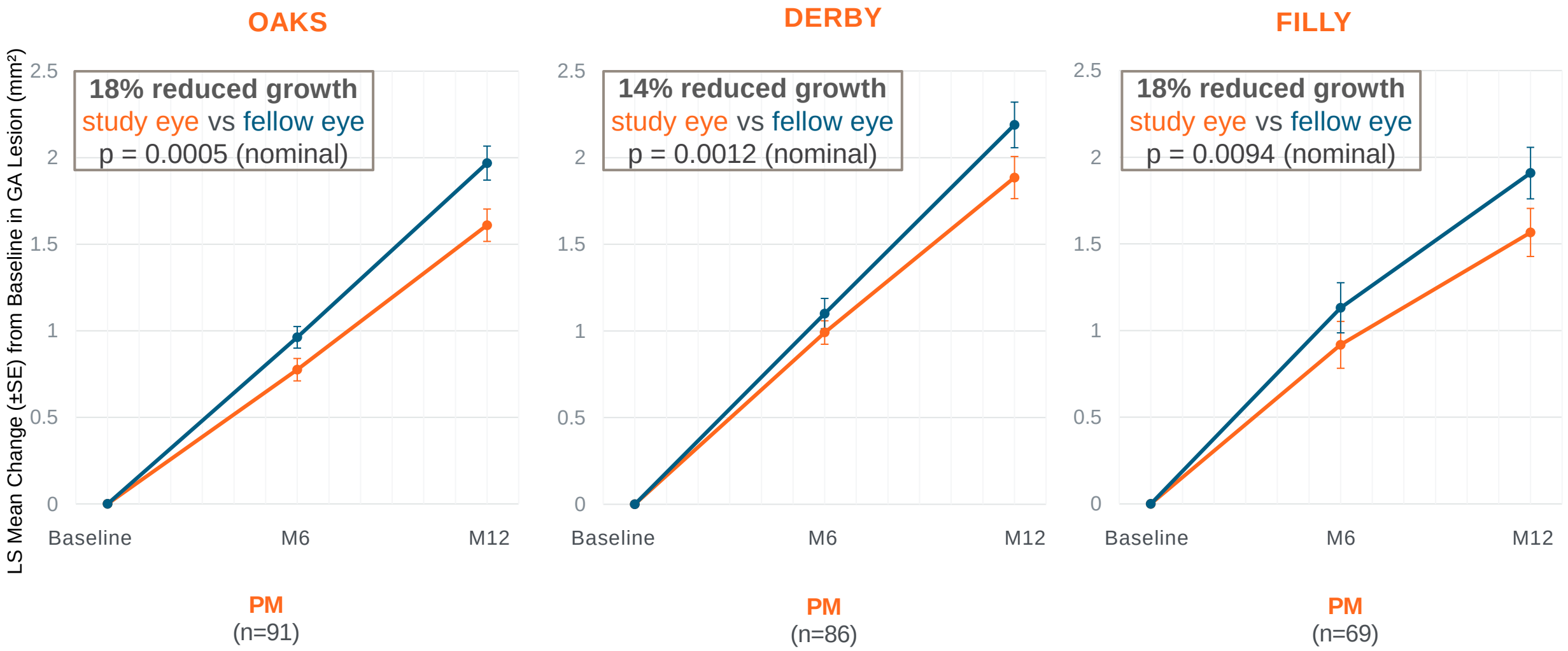
Pegcetacoplan **monthly** reduced lesion growth in treated study eyes vs. untreated fellow eyes



LS means estimated from a mixed-effects model for repeated measures. The mITT population was used for the analysis.
GA=geographic atrophy; LS=least square; M=month; PEOM=pegcetacoplan every other month; PM=pegcetacoplan monthly; SE=standard error.

Conclusions

- Pegcetacoplan monthly and every other month met the primary endpoint in OAKS
- Pegcetacoplan monthly and every other month did not meet the primary endpoint in DERBY
- Pegcetacoplan demonstrated greater efficacy in patients with extrafoveal lesions at baseline
- OAKS, DERBY, and FILLY all show consistent efficacy of pegcetacoplan in treated study eyes versus untreated fellow eyes
- The pegcetacoplan GA development program includes over 1,500 patients across OAKS, DERBY, and FILLY, collectively demonstrating slowing of GA progression by pegcetacoplan monthly and every other month

GA=geographic atrophy.